inorganic, organic and polymer materials suitable for microparticle enhanced light scattering assays and are coated with a first binding partner for said analyte, and second microparticles having a mean diameter and a refractive index, wherein said second microparticles are selected from the group consisting of inorganic, organic and polymer materials suitable for microparticle enhanced light scattering assays and are coated with a second binding partner for said analyte, said first microparticles having stronger light scattering properties than said second microparticles, and said first binding partner coated upon said first microparticles having a higher reactivity for said analyte than said second binding partner coated upon said second microparticles, said microparticles being capable of causing light scattering at wavelengths suitable for the detection of agglutinated microparticles.

## REMARKS

Claims 1- 17 and 20 remain active in this application. Reconsideration is again respectfully requested.

In an effort to conclude the prosecution of the above-identified patent application, Claims 19 and 21 are canceled and Claim 1 amended to more particularly define Applicants' invention. Claim 1 as amended recites that the material comprising the microparticles making up the novel agglutination assay reagent of the invention are selected from the group consisting of inorganic, organic and polymer materials suitable for microparticle enhanced light scattering assays. Further, Claim 1 recites that the microparticles are capable of causing light scattering at wavelengths suitable for the detection of agglutinated microparticles. Clearly, Applicants' reagent would not be suitable for such an assay were the particles not of suitable material therefor. Support for the designation of the material utilized to form the subject microparticles is to be found at page 9, lines 10 and 11. Support for the statement that the microparticles of the

claimed reagent are capable of causing light scattering at wavelengths suitable for the detection of agglutinated microparticles is to be found at page 8, lines 3 and 4 of Applicants' specification. This foregoing amendments to Claim 1 are made at this time in answer to the Examiner's stated position in the Final Office Action that the preamble of the claims is not sufficient to render them patentable over the citations of record. The amendment more precisely defines Applicants' invention and does not introduce new matter therein. Given the justification for the submission of the amendments at this time, entry thereof is clearly warranted and is therefore respectfully requested.

The rejection of Claims 1-8 and 10-12 under 35 U.S.C. §103(a) as being unpatentable over Grange *et al.* in view of Lindmo *et al.* is respectfully traversed. All rejections encompassing Claims 19 and 21 not previously withdrawn are obviated by their cancellation and will not be further mentioned herein. Grange *et al.*, as correctly noted in the Office Action under reply, teach agglutination assays in which antigens and antibodies are covalently bound to light scattering particles and analyte concentration is measured by nephelometry. Regardless of the other general similarities between the overall teaching of Grange *et al.* and Applicants' invention noted in the Office Action under reply, there is a fundamental difference and distinction between them that is also correctly pointed out in the Office Action under reply. Grange *et al.* fails render to render the Claims under consideration unpatentable because it neither teaches nor suggests differential characterization between microparticles of specific size populations, differential reactivity and dissociation constants between two immunological binding partners. Since the teachings of Grange *et al.* fail to suggest the diagnostic methodology of Applicants' invention, it is respectfully submitted that no motivation can be drawn therefrom for one of ordinary skill in the art to prepare the reagents as claimed in Claims 1-17 and 20.

In implicit recognition of the deficiency in the teachings of Grange *et al.*, Lindmo *et al.* is combined therewith in making the rejection. It is respectfully submitted, however, that the two are not properly combinable. Lindmo *et al.* teach an assay based on flow cytometry, which is based on totally different principles than microparticle-

enhanced light scattering agglutination assays. In assays by flow cytometry, there is no aggregation of microparticles and the amount of soluble labeled antibody is determined for each particle individually as they are separated and, possibly, also by distinguishing characteristics if such exist and are detectable by the flow cytometer. Because Grange *et al.* and Lindmo *et al.* teach assays that are based on clearly distinct principles, it is respectfully submitted that there would be no motivation for one of ordinary skill in the art to combine them to create the novel reagents of the Claims under consideration.

The assays taught by Lindmo *et al.* do not require reagents that possess light scattering capabilities. More important, since the assay of Lindmo *et al.* is based on principles unrelated to those for which the claimed reagent is suitable, there would be absolutely no suggestion therein for one or ordinary skill in the art to prepare a reagent possessing light scattering capabilities at wavelengths suitable for the detection of agglutinated microparticles. Clearly, since the assay taught by Lindmo *et al.* does not involve agglutination, there would be no teaching therein from which one of ordinary skill in the art would be motivated to create such particles. Hence, it is respectfully submitted that the teachings of Grange *et al.* are not properly combinable with Lindmo *et al.*.

In support of her position, the Examiner contends, in part, that the preamble of a claim cannot render them patentable citing *Ex parte* Masham. Applicants respectfully disagree and find the Masham decision inappropriate. In Masham, the claimed invention was a mechanical mixing apparatus intended for mixing flowing developer material and the prior art device was intended for the same purpose. In the present invention, the issue is motivation to combine the teachings of two separate citations that teach, not the same purpose, but uses that are clearly distinct and are based on different principles. Hence, it is submitted that Masham is not controlling. It is submitted that a reagent and its properties cannot be separated for purposes of making a rejection when the properties thereof are inherent and where the properties, specifically the utility of the reagent, is the fundamental distinction that would not suggest combining the teachings of the two citations to arrive at the claimed invention. The foregoing

amendments, however, render the point moot since the claims recite that the microparticles possess a property clearly outside of the scope and purpose of the teachings of Lindmo *et al.* withdrawal of the rejection is clearly in order and is respectfully requested.

The rejection of Claim 9 under 35 U.S.C. §103(a) as being unpatentable over Grange *et al.* in view of Lindmo *et al.*, further in view of Sutton *et al.* is respectfully traversed. Grange *et al.* and Lindmo *et al.* have been discussed above. It has been established that one of ordinary skill in the art would not be led to create the reagents of the Claims under consideration by combining their teachings because the assays they describe are based on different principles. Sutton *et al.* teaches specific copolymers coated on the surface of insoluble particles and having covalently bound thereto an oligonucleotide complimentary to a nucleic acid analyte. Such a teaching is respectfully submitted to be unrelated to the assay taught by Lindmo *et al.* and does not render Claim 9 unpatentable in combination with Grange *et al.* since it does not cure the deficiencies of Grange *et al.* as it applies to Claim 1. Therefore, based only on the fact that Sutton *et al.* teaches the use of oligonucleotide capture probes for a nucleic acid analyte, which is known in the art, it is respectfully submitted that one of ordinary skill in the art would not be led to create the reagent of Claim 9 by combining the teachings of Sutton *et al.* with Grange *et al.* and certainly not by combining the teachings of Sutton *et al.* with either Lindmo *et al.* or Lindmo *et al.* and Grange *et al.* since their teachings are not combinable as pointed out above. Withdrawal of the rejection is respectfully requested.

The rejection of Claims 13-17 and 20 under 35 U.S.C. §103(a) as being unpatentable over Grange *et al.* in view of Lindmo *et al.* further in view of Harchali *et al.* is respectfully traversed. Grange *et al.* and Lindmo *et al.*, and their respective shortcomings, have been discussed above. It has been established that one of ordinary skill in the art would not be led to create the reagents of the Claims under consideration by combining their teachings because they operate on different principles. Harchali *et al.* is cited as a teaching of polyacrylic, polyfunctional, copolymerized microparticles

conjugated with antigens of defined epitopic specificity, used "in an agglutination essay". The assay of the citation, in distinct contrast to that of the claims under consideration, is based on the absence of agglutination. Hence, one of ordinary skill in the art seeking new reagents useful in agglutination reactions and possessing light scattering capabilities at wavelengths suitable for the detection of agglutinated microparticles would not look to the teachings of Harchali *et al.* and would certainly have no motivation to combine their teachings with either Grange *et al.* or Lindmo *et al.*, particularly the latter. Withdrawal of the rejection is in order and is respectfully requested.

Accordingly, it is respectfully submitted that, as Claims 1-17 and 20 clearly define patentable subject matter over the citations cited of record, this application is in condition for allowance. An early Notice of Allowance is courteously solicited.

In the event the Examiner deems a further discussion of this application would expedite prosecution to allowance, the undersigned Attorney of Record would welcome the opportunity to hold such a discussion. The Examiner's cooperation in this regard would be greatly appreciated.

Respectfully submitted,

Diane L. Ferrone
Registration No. 36,135
Attorney for Applicant
Phone (973) 596-4879

Date Sept 3, 2002

Please address all communications to:
Intellectual Property Docket Administrator
Gibbons, Del Deo, Dolan, Griffinger & Vecchione
One Riverfront Plaza
Newark, New Jersey 07102-5497

**AMENDED CLAIMS WITH MARKINGS TO SHOW CHANGES MADE**

1.(Amended) A reagent for performing an agglutination assay for determining the amount of an analyte in a sample, said reagent comprising **[: a.]** a mixture of microparticles, said mixture comprising first microparticles having a mean diameter and a refractive index, wherein said first microparticles are **selected from the group consisting of inorganic, organic and polymer materials suitable for microparticle enhanced light scattering assays and are** coated with a first binding partner for said analyte, and second microparticles having a mean diameter and a refractive index, wherein said second microparticles are **selected from the group consisting of inorganic, organic and polymer materials suitable for microparticle enhanced light scattering assays and are** coated with a second binding partner for said analyte, **[and]** said first microparticles having stronger light scattering properties than said second microparticles, and said first binding partner coated upon said first microparticles having a higher reactivity for said analyte than said second binding partner coated upon said second microparticles**, said microparticles being capable of causing light scattering at wavelengths suitable for the detection of agglutinated microparticles**.